HUMAN TRAITS

Trait Dominant (DD or Dd) Recessive (rr)

Digits on fingers & toes extra normal

Dimpled cheeks present absent

Earlobes free attached

finger length short, stubby normal

hairline widow’s peak straight

hair form curly straight

mid-digital hairs present absent

palate cleft normal

skin pigment normal albino

taste ability PTC taster PTC non-taster

thumb hitch - hiker (?) straight

toe length 2nd toe longest big toe longest

Tongue musculature control can roll cannot roll

Pigmented iris pigment non-pigment (blue)

little finger bend turned toward ring finger straight

double jointed thumb loose ligaments tight ligaments

color vision normal color blind

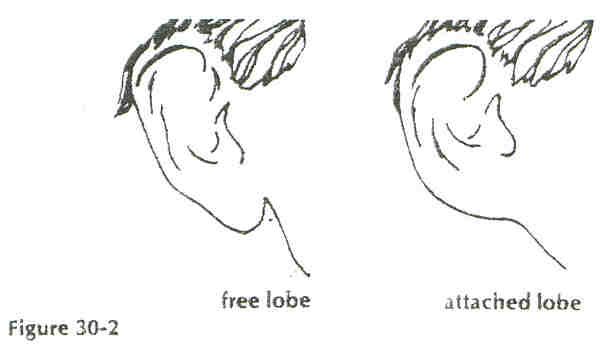
**Pedigree Studies**

Pedigrees are not reserved for show dogs and racing horses. All living things, including you, have pedigrees. A pedigree is a diagram that shows the occurrence and appear­ance, or phenotype, of a particular genetic trait from one generation to the next in a family. Genotypes for individuals in a pedigree can usually be determined with knowl­edge of inheritance and probability.

In this investigation, it is expected that you:

(a) learn the meaning of all symbols and lines that are used in representing a pedigree.

(b) predict genotypes for all individuals shown in two sample pedigrees

**Procedure:**

The pedigree in Figure 30-1 shows the pattern inheritance in a family for a specific trait. The trait being shown is ear lobe shape. Geneticists recognize two general ear lobe shapes, free lobes and attached lobes (Figure 30-2). The gene re­sponsible for free lobes (E) is dominant over the gene for attached lobes (e).

In a pedigree, each generation is represented by a Roman numeral. Each person in a gener­ation is numbered. Thus each person can be iden­tified by his generation numeral and number. Males are represented by square symbols while females are represented by round symbols (Fig­ure 30-1).

All darkened symbols on a pedigree represent individuals who are homozygous recessive for the trait being studied. Therefore, persons I-1 and II­-2 have ee genotypes. They are the only two indi­viduals who are homozygous recessive and show the recessive trait. They have attached ear lobes.

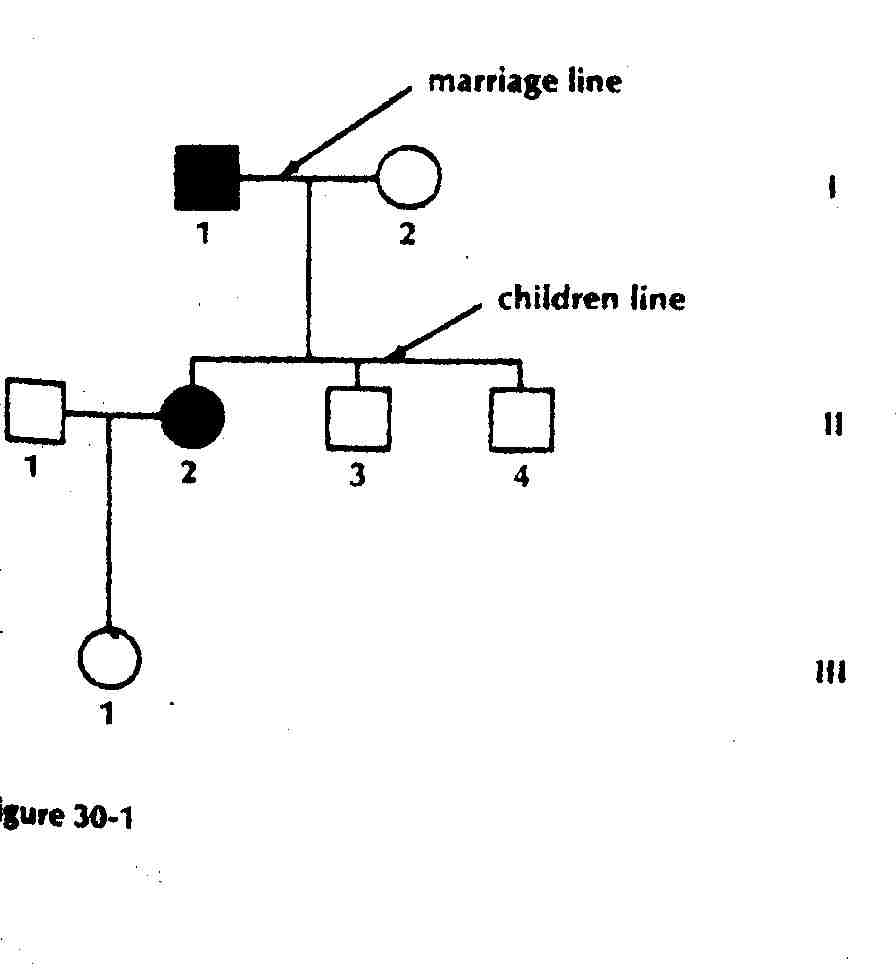
All undarkened symbols have at least one dom­inant gene (E). The genotype for person 1-2 is ei­ther EE or Ee. How can you determine which it is? Punnett squares can be used to aid in deter­mining the genotypes. If the mother (I-2) is EE, then a Punnett square such as the one in Figure 30-3 results in all children having free ear lobes. Do the pedigree symbols for the children support this? \_\_\_\_

Because one child has attached ear lobes, person I-2 must be Ee. .

What are the genotypes for, children II-3 an II-4? Since they have free ear lobes, II-3 and II-4 can only be Ee because the father is ee and the mother is Ee.

Because he has free ear lobes, person II-1 (husband of oldest daughter) may be EE or Ee. All children would be Ee (free lobes) if the father were EE (Figure 30-3). Does the pedigree support this? \_\_\_\_ If the father were Ee, half the children would probably have attached ear lobes (ee) (Figure 30-4). Does the pedigree support this? \_\_\_\_

There are not enough children to make a definite conclusion. With only one child, either ge­notype is possible for the father. Therefore, his genotype is shown as E?.

* Using the same genes as above for ear lobe shape, determine the genotypes of all individuals in family A (Figure 30-5) and family B (Figure 30-6).
* Record the genotypes of each person on the line below his number in the pedigree. The answers for family A are given below.

Answers for family A:

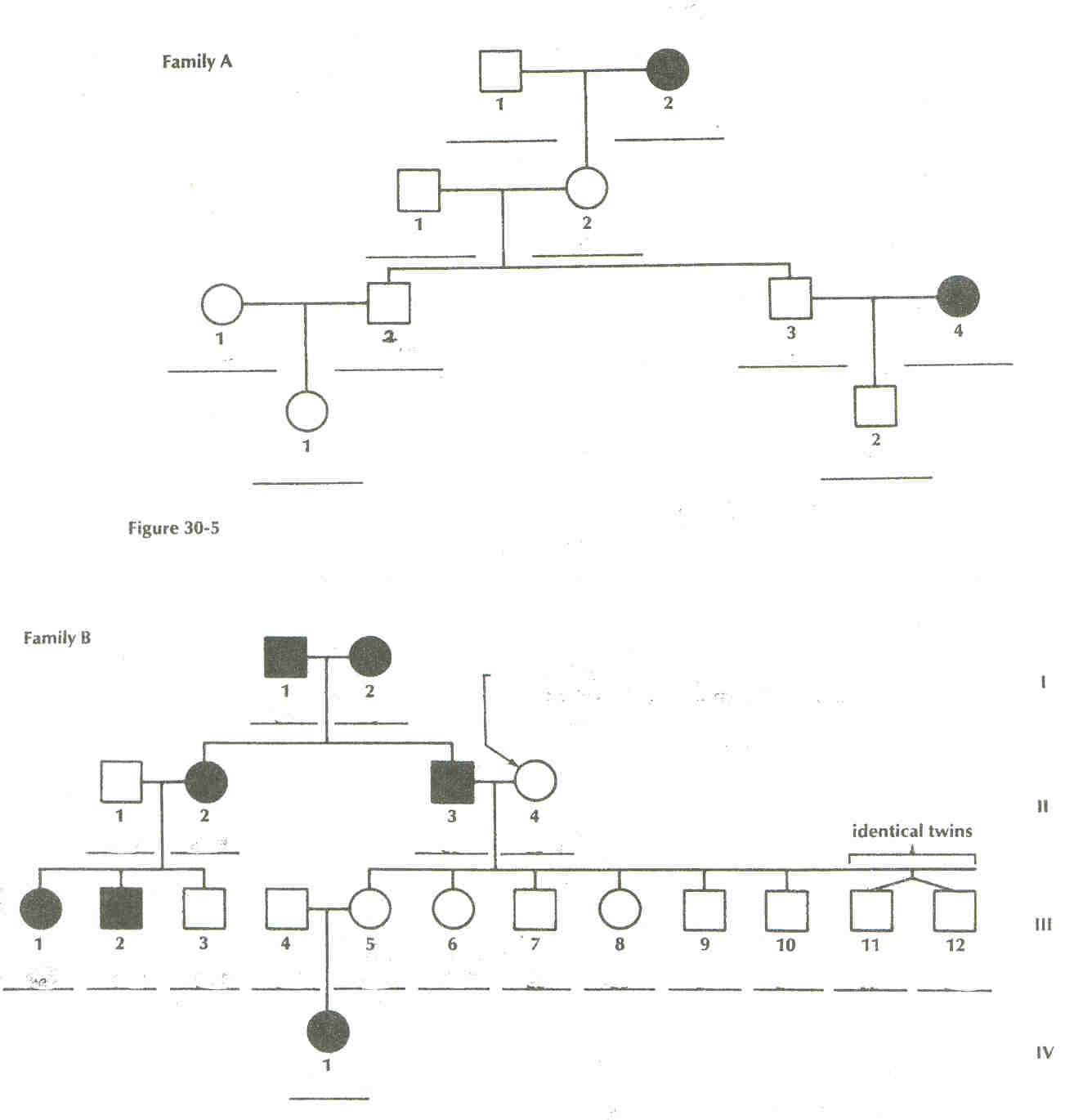
I-1 = E? III-2 = E?

I-2 = ee III-3 = E?

II-1 = E? III-4 = ee

II-2 = Ee IV-1 = E?

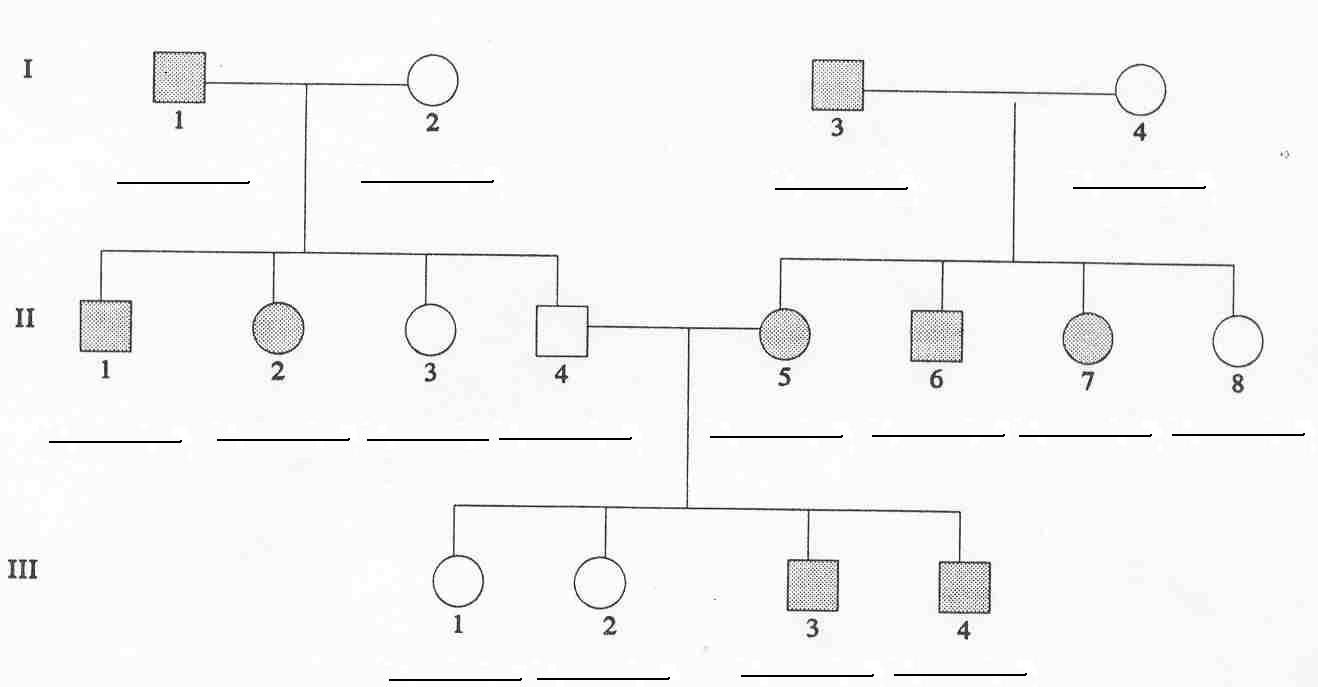
III-1 = E? IV-2 = Ee

1. Recopy Figure 30-5 (Family A). However, the following changes are to be made: person II-2 and III-3 only are to be shaded in. DO NOT shade in I-2 or III-4. Using ear lobe shape, indicate genotypes for all individuals in this pedigree.

2. Recopy Figure 30-6 (Family B). However, the following changes are to be made: Person I-1, II-4, III-2, 5, 6, 8, 9, and 10 only are to be shaded in. DO NOT shade in I-2, II-2, 3, III-1, or IV-1. Using ear lobe shape, indicate genotypes for all individuals in this pedigree.

**CONCLUSIONS:**

Answer the conclusion questions below based on the following pedigree chart that shows the appearance of the tongue rolling trait in a family.



**1. List the genotypes of each individual in the pedigree chart.**

**2. If individuals 4 and 5 in generation II have another child, what is the probability that it will be a roller? Explain.**

**3. If individual 8 in generation II were to marry a man who is homozygous domi­nant for tongue rolling, what is the probability that their first child will be a non-roller? Explain.**

## Below is a set of problems dealing with sex-linked traits. For each problem, do a Punnett square to help you answer the question.

## Sex-Linked Inheritance Problem Set

The study of inheritance of genes located on sex chromosomes was pioneered by T. H. Morgan and his students at the beginning of the 20th century. Although Morgan studied fruit flies, the same genetic principles apply to humans. Since males and females differ in their sex chromosomes, inheritance patterns for X-chromosome linked genes vary between the sexes. Our objective is to understand the principles that govern inheritance of genes on sex chromosomes.

**Instructions:** The following problems have multiple choice answers. Correct answers are reinforced with a brief explanation. Incorrect answers are linked to tutorials to help solve the problem.

1. [Crossing a white-eyed female and red-eyed male fly](http://www.biology.arizona.edu/mendelian_genetics/problem_sets/sex_linked_inheritance/01Q.html)
2. [Test cross of a red-eyed female fly](http://www.biology.arizona.edu/mendelian_genetics/problem_sets/sex_linked_inheritance/02Q.html)
3. [Predicting the offspring of a homozygous red-eyed female fly](http://www.biology.arizona.edu/mendelian_genetics/problem_sets/sex_linked_inheritance/03Q.html)
4. [Predicting genotype when phenotype is known](http://www.biology.arizona.edu/mendelian_genetics/problem_sets/sex_linked_inheritance/04Q.html) OMIT THIS ONE
5. [Another white-eyed female x red-eyed male fly cross](http://www.biology.arizona.edu/mendelian_genetics/problem_sets/sex_linked_inheritance/05Q.html)
6. [Hemophilia in humans](http://www.biology.arizona.edu/mendelian_genetics/problem_sets/sex_linked_inheritance/06Q.html)
7. [Red-green color blindness in humans](http://www.biology.arizona.edu/mendelian_genetics/problem_sets/sex_linked_inheritance/07Q.html)
8. [Tracing the inheritance of the human Y chromosome](http://www.biology.arizona.edu/mendelian_genetics/problem_sets/sex_linked_inheritance/08Q.html)
9. [Tracing the inheritance of the human X chromosome](http://www.biology.arizona.edu/mendelian_genetics/problem_sets/sex_linked_inheritance/09Q.html)
10. [Offspring of human females who are carriers for X-linked traits](http://www.biology.arizona.edu/mendelian_genetics/problem_sets/sex_linked_inheritance/10Q.html)

For the song below, access the Fourth Nine Weeks folder and play the song “I am MY Own Grandpa”. Complete a pedigree for this song and turn it in.

I'm My Own Grandpa!

Many, many years ago

When I was twenty three,

I got married to a widow

Who was pretty as could be,

This widow had a daughter  
Who had hair of red.  
My father fell in love with her,  
And soon the two were wed.

This made my dad my son‑in‑law  
And changed my very life.  
My daughter was my mother,  
For she was my father's wife.

To complicate the matters worse,  
Although it brought me joy,  
I soon became the father  
Of a bouncing baby boy.

My little baby then became  
A brother‑in‑law to dad.  
And so became my uncle,  
Though it made me very sad.

For if he was my uncle,  
Then that also made him brother  
To the widow's grown‑up daughter  
Who, of course was my step‑mother.

Father's wife then had a son,  
Who kept them on the run.  
And he became my grandson,  
For he was my daughter's son.

My wife is now my mother's mom.  
And it surely makes me blue.  
Because, although she is my wife,  
She is my grandma too.

If my wife is my grandmother,  
Then I am her grandchild.  
And every time I think of it,  
It simply drives me wild.

For now I have become  
The strangest case you ever saw.  
As the husband of my grandmother,  
I am my own Grandpa

**Hemophilia: "The Royal Disease"**

by Yelena Aronova-Tiuntseva and Clyde Freeman Herreid  
University at Buffalo, State University of New York

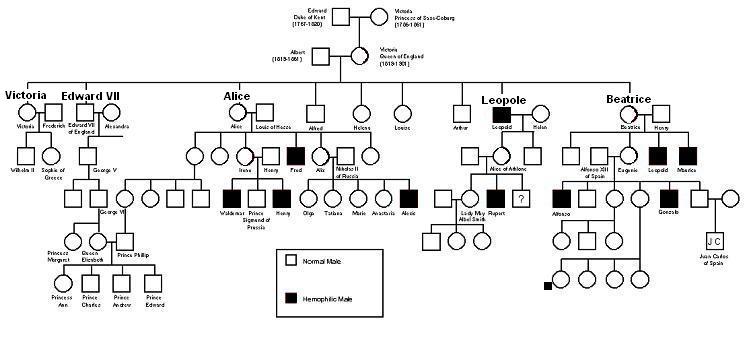
Hemophilia is an X-linked recessive disorder characterized by the inability to properly form blood clots. Until recently, hemophilia was untreatable, and only a few hemophiliacs survived to reproductive age because any small cut or internal hemorrhaging after even a minor bruise was fatal. Now hemophilia is treated with blood transfusions and infusions of a blood derived substance known as anti-hemophilic factor. However, such treatment is very expensive and involves the risk of contracting AIDS.

Hemophilia affects males much more frequently (1 in 10,000) than females (1 in 100,000,000). This occurs because a critical blood clotting gene is carried on the X chromosome. Since males only carry one X chromosome, if that is defective, hemophilia will immediately show up. An early death is likely. Females, on the other hand, carry two X chromosomes. If only one is defective, the other normal X chromosome can compensate. The woman will have normal blood clotting; she will simply be a carrier of the recessive defective gene. This fact will be discovered if some of her children are hemophiliacs. Naturally, women hemophiliacs are rare because it takes two defective X chromosomes in order for the condition to be seen.

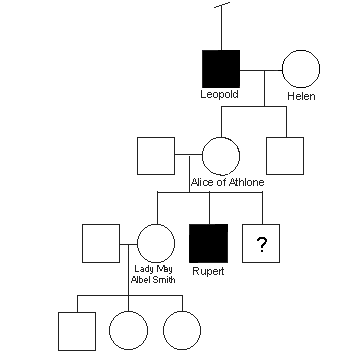
Hemophilia has played an important role in Europe's history, for it suddenly cropped up in the children of Great Britain's Queen Victoria. It became known as the "Royal disease" because it spread to the royal families of Europe through Victoria's descendants. Queen Victoria had always been worried about the quality of the blood of the British royal family. Her feelings about the necessity of revitalizing what she called the "lymphatic" blood of their houses are reflected in her letter to her daughter Vicky: "I do wish one could find some more black eyed Princes and Princesses for our children! I can't help thinking what dear Papa said -- that it was in fact when there was some little imperfection in the pure Royal descent that some fresh blood was infused... For that constant fair hair and blue eyes makes the blood so lymphatic... it is not as trivial as you may think, for darling Papa -- often with vehemence said: "We must have some strong blood."

It is doubtful that at the time of writing this letter, the Queen knew exactly what was wrong with her family's blood. Hemophilia first appeared in Victoria's family in her eighth child, Prince Leopold, Duke of Albany. Throughout his short life, Leopold had suffered severe hemorrhages, and always was described as "very delicate." Leading the life of a normal youngster was impossible for Leopold because any cut or bump could lead to death and it was necessary to keep him always under strict surveillance. However, in spite of all the protection, Prince Leopold died at the age of thirty-one as the result of a minor fall.

The appearance of hemophilia in one of Victoria's sons upset and confused the Queen, who could only protest that the disease did not originate in her side of the family. Yet, a whisper about the "curse of the Coburgs" was spread about. This curse was supposed to have dated from the early nineteenth century, when a Coburg prince had married a Hungarian princess named Antoinette de Kohary. A monk, a member of the Kohary family, envied the wealth inherited by the happy couple from the bride's father, and cursed future generations of Coburgs with the disease. Of course, hemophilia affecting Victoria's offspring had nothing to do with the curse. The traditional view is that there was a mutation in either her or in a sperm of her father, Edward Augustus, Duke of Kent. From there it spread through the Royal Houses of Europe as monarchs arranged marriages to consolidate political alliances. We can trace the appearance of hemophilia as it popped up in Spain, Russia, and Prussia by looking at the family tree.



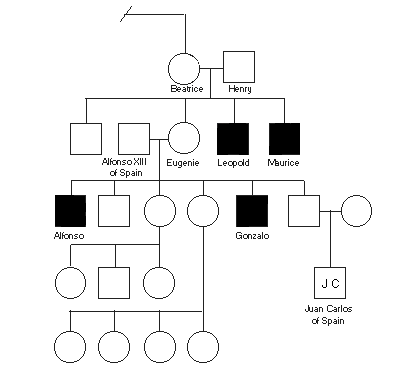
1. First, let's take a look at Queen Victoria's son Leopold's family. His daughter, Alice of Athlone, had one hemophilic son (Rupert) and two other children -- a boy and a girl -- whose status is unknown. a) What is the probability that her other son was hemophilic? b) What is the probability that her daughter was a carrier? hemophiliac? c) What is the probability that both children were normal?



Fortunately, Leopold was the only one of Victoria's sons who suffered from hemophilia. Her other three sons, Edward, Alfred, and Arthur, were unaffected. Since the present royal family of England descended from Edward VII, the first son, it is free from hemophilia.

Louise, Queen Victoria's fourth daughter and sixth child, did not have children and her status as a carrier cannot be assessed. Vicky, the first child, and Helena, the fifth child, had children, none of whom was hemophilic, indicating that the mothers probably were not carriers.

1. Now for the Spanish connection: Victoria's youngest child, Beatrice, gave birth to one daughter, one normal son, and two hemophilic sons. Looking at the pedigree of the royal family, identify which of Beatrice's children received the hemophilic gene; why can you make this conclusion? Notice that Beatrice's daughter, Eugenie, married King Alfonso XIII of Spain and had six children, one of whom was the father of Juan Carlos, the current King of Spain. Would you predict that Juan Carlos was normal, a carrier, or a hemophilic?



1. Queen Victoria's third child, Alice, passed hemophilia to the German and Russian imperial families. Of Alice's six children, three were afflicted with hemophilia. At the age of three, her son Frederick bled for three agonizing days from a cut on the ear. Eventually, the flow of blood was stanched. But a few months later, while playing boisterously in his mother's room, the boy charged headlong through an open window and fell to the terrace below. By the evening he was dead from the internal bleeding.

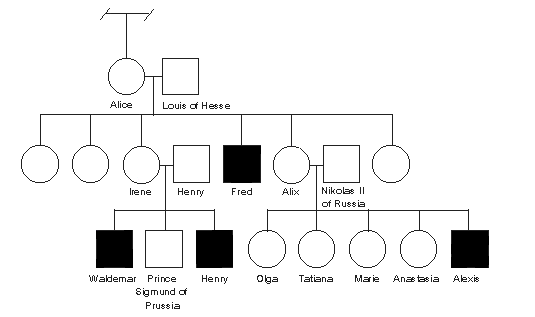
Alice's daughter Irene, a carrier, married her first cousin, Prince Henry of Prussia, and gave birth to two hemophilic sons. Every attempt was made to conceal the fact that the dreaded disease had shown itself in the German imperial family, but, at the age of four, Waldemar, the youngest of the princes, bled to death. The other prince, Henry, died at the age of fifty-six.

Alice's other daughter, Alix, was also a carrier. Had she accepted the offer of marriage from Prince Eddy, or his brother George, hemophilia would have been re-introduced into the reigning branch of the British royal family. But Alexandra (Alix) married Tsar Nikolas II instead and carried the disease into the Russian imperial family. She had four daughters, Olga, Tatiana, Marie, and Anastasia, before giving birth to the long-awaited son, Alexis, heir to the Russian throne. These children, along with their parents, were eventually murdered during the Russian Revolution.

Within a few months of his birth, his parents realized that their precious and only son, Alexis, had hemophilia. The first sign had been some unexpected bleeding from the navel, which had stopped after a few days. Much more serious, however, were the dark swellings that appeared each time the child bumped an arm or a leg. And worst of all was the bleeding into the joints. This meant a crippling of the affected limbs in addition to excruciating pain. As the boy grew older, he was obliged to spend weeks in bed, and after he was up, to wear a heavy iron brace.

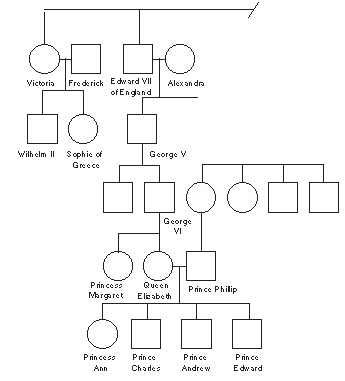
Neither well-experienced doctors nor numerous prayers to God by desperate parents seemed to help the suffering child. Distressed over their son's condition, his parents, the Tsar and Tsarina, turned to the monk Rasputin, a spiritualist who claimed he could help Alexis. Rasputin received an unlimited trust from Alexandra because he was the only person who was able to relieve her son's sufferings. How he managed to do this is uncertain. "A likely explanation is that Rasputin, with his hypnotic eyes and his self-confident presence, was able to create the aura of tranquility necessary to slow the flow of blood through the boys veins. Where the demented mother and the dithering doctors merely increased the tenseness of the atmosphere around the suffering child, Rasputin calmed him and sent him to sleep." While Tsar and Tsarina were preoccupied with the health of their son, the affairs of state deteriorated, culminating in the Russian revolution.

Alexis did not die from hemophilia. At the age of fourteen he was executed with the rest of the family. His four oldest sisters were also young and didn't have children, so we don't know whether any of them was a carrier. But we can make an estimate. a) What are the probabilities that all four of the girls were carriers of the allele hemophilia? b) Suppose Alexis had lived and married a normal woman, what are the chances that his daughter would be hemophilic? c) What are the chances his daughters would be carriers? d) What are the chances that his sons would be hemophiliacs?



1. In 1995, a sixty-three year old man named Eugene Romanov, a resident of the former Soviet Union, turned up. He shared both the disease and his last name with the royal family of czarist Russia. He proclaimed himself a grandson of Nikolas II's youngest daughter, Anastasia, whose body had never been recovered, and who was believed by some to have managed to survive the revolution. Eugene Romanov claimed Anastasia was raised by a farmer, and later she married a nephew of her adopted parents and had a daughter, Eugene's mother. a) According to Eugene's argument, what was the likely hemophilic status of Eugene's mother and grandmother? What about his father and grandfather? Is this argument plausible? b) How plausible is it that Eugene inherited both hemophilia and the last name from the royal family? (Hint: Look how each of them is passed from generation to generation.)
2. Prince Charles is the designated next king of England. His well publicized marriage to Princess Diana has now ended in an acrimonious divorce, leaving two boy children. If you learned that one of the two was a hemophiliac, what are the possible explanations for this event?

Finally, our speculative natures compel us to mention that in 1995 two British brothers produced a new book (*Queen Victoria's Gene*) with a breathtaking suggestion. Professors Malcolm Potts, an embryologist at Berkeley, and William Potts, a zoologist at Britain's Lancaster University, suggest that Queen Victoria might have been illegitimate. They point out that neither her father nor her husband was a hemophiliac. So either there was a spontaneous mutation - a one-in-50,000 chance - or Victoria is the daughter of someone other than the Duke of Kent. Think of the possible consequences to European history: No Victoria, and the current Prince of Hanover, Ernst (descendent of the brother of Victoria's father), would be King of England today. More importantly, no Victoria would mean no hemophilic son of the Czar of Russia, no Rasputin, and no revolution? What are the chances of this scenario?

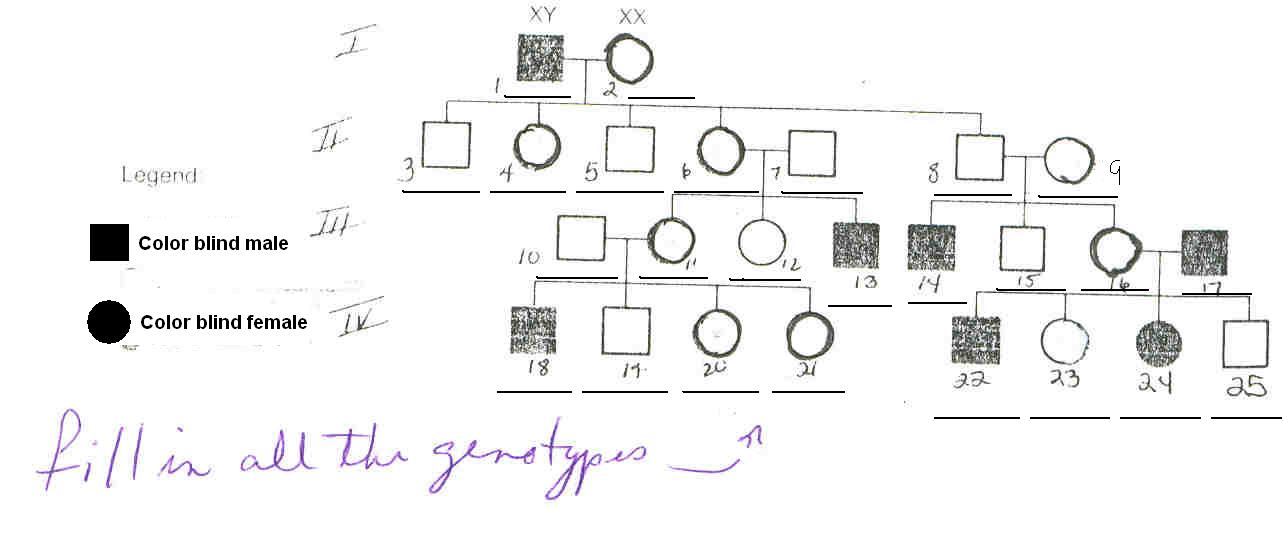
**QUESTIONS FOR DISEASE OF ROYALTY**

**1. Who was affected (carrier) in the beginning of the documentation?**

**2. Why would Albert not be the carrier?**

**3. How did Alexis have hemophilia?**

**4. What are the chances of the current royal family of England having children with hemophilia today?**

****

**QUESTIONS FOR COLOR BLINDNESS IN A FAMILY (13.7)**

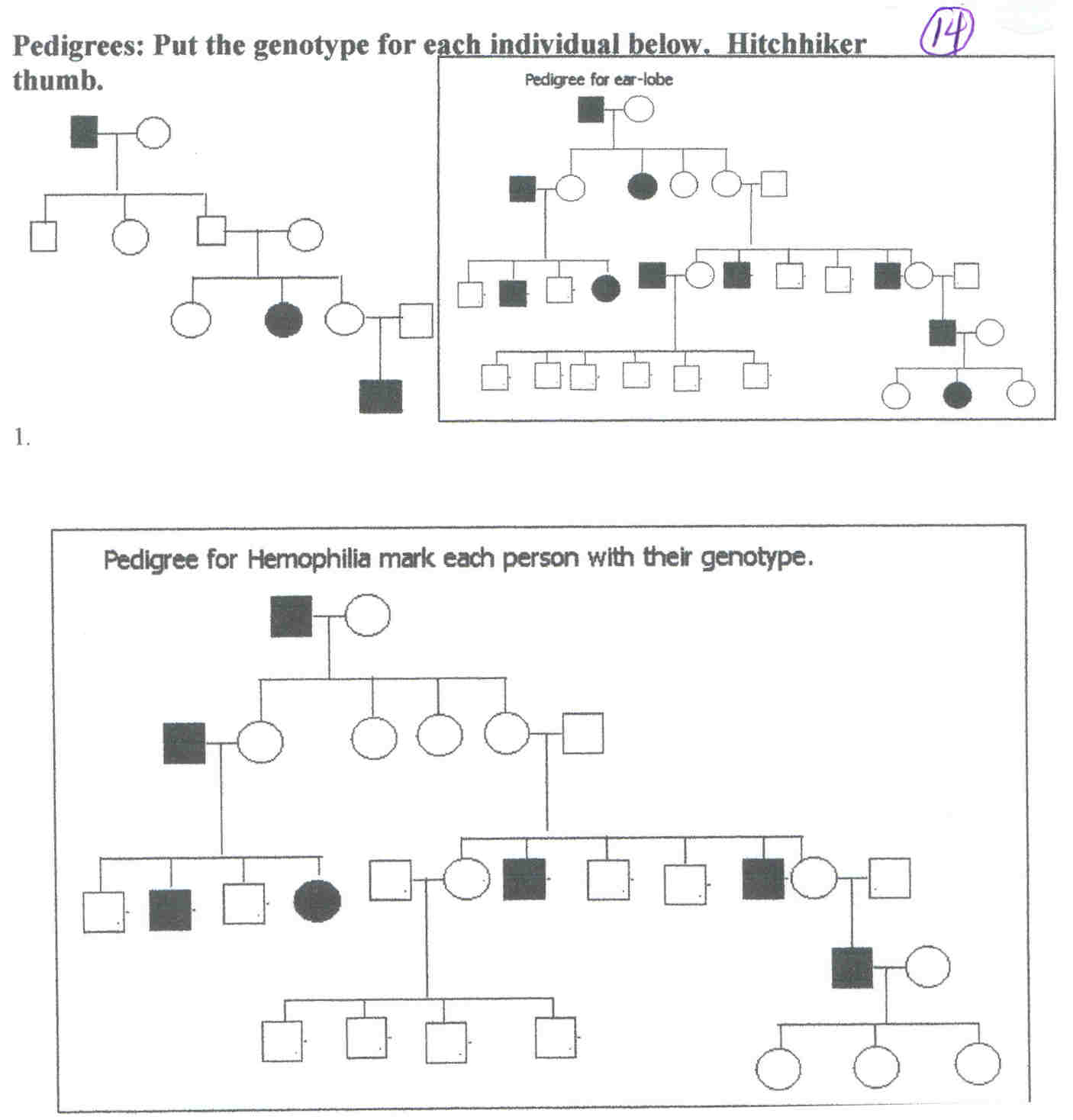
**1. Were there any color blind children in the second generation?**

**2. When did a color blind child occur first?**

**3. Give the numbers of the carriers and identify whether they are male or female.**

**4. Give the numbers of the affected color blind people and identify whether they are male or female.**

**5. Based on this family, what type of disorder would color blindness be classed as? Why?**



## Karyotyping Activity

This exercise is a simulation of human karyotyping using digital images of chromosomes from actual human genetic studies. You will be arranging chromosomes into a completed karyotype, and interpreting your findings just as if you were working in a genetic analysis program at a hospital or clinic. Karyotype analyses are performed over 400,000 times per year in the U.S. and Canada. Imagine that you were performing these analyses for real people, and that your conclusions would drastically affect their lives.

**G Banding**

During mitosis, the 23 pairs of human chromosomes condense and are visible with a light microscope. A karyotype analysis usually involves blocking cells in mitosis and staining the condensed chromosomes with Giemsa dye. The dye stains regions of chromosomes that are rich in the base pairs Adenine (A) and Thymine (T) producing a dark band. A common misconception is that bands represent single genes, but in fact the thinnest bands contain over a million base pairs and potentially hundreds of genes. For example, the size of one small band is about equal to the entire genetic information for one bacterium.

|  |  |
| --- | --- |
|  |  |

The analysis involves comparing chromosomes for their length, the placement of centromeres (areas where the two chromatids are joined), and the location and sizes of G-bands. You will electronically complete the karyotype for three individuals and look for abnormalities that could explain the phenotype.

**Your assignment**

This exercise is designed as an introduction to genetic studies on humans. Karyotyping is one of many techniques that allow us to look for several thousand possible genetic diseases in humans.

You will evaluate 3 patients' case histories, complete their karyotypes, and diagnose any missing or extra chromosomes. Then you'll conduct research on the internet to find web sites that cover that aspect of human genetics. For this assignment, you should turn in a total of 7 answers on paper (2 for each patient, 1 for the internet search).

[](http://www.biology.arizona.edu/Human_Bio/activities/karyotyping/karyotyping2.html)

**As you READ the accompanying article, draw a pedigree for the Fugate family. As genetic councilors, you will have some gaps in your knowledge. Affected individuals should be colored in and carriers should be half colored in.**

**THE BLUE PEOPLE OF TROUBLESOME CREEK**

**The story of an Appalachian malady, an inquisitive doctor, and a paradoxical cure. by Cathy Trost Illustrations by Walt Spitzmiller**

Six generations after a French orphan named , Martin Fugate settled on the banks or eastern Kentucky's Troublesome Creek with his red­ headed American bride, his great-great-great­ great grandson was born in a modern hospital not far from where the creek still runs. The boy inherited his father's lankiness and his mother's slightly nasal way of speaking.

What he got from Martin Fugate was dark blue skin. "It was almost purple," his father recalls.

Doctors were so astonished by the color of Benjy Stacy's skin that they raced him by ambulance from the maternity ward in the hospital near Hazard to a med­ical clinic in Lexington. Two days of tests produced no explanation for skin the color of a bruised plum.

A transfusion was being prepared when Benjy's grand­mother spoke up. "Have you ever heard of the blue Fugates of Troublesome Creek?" she asked the doctors.

"My grandmother Luna on my dad's side was a blue Fugate. It was real bad in her," Alva Stacy, the boy's fa­ther, explained. "The doctors finally came to the con­clusion that Benjy's color was due to blood inherited from generations back."

Benjy lost his blue tint within a few weeks, and now he is about as normal looking a seven-year-old boy as you could hope to find. His lips and fingernails still turn a shade of purple-blue when he gets cold or angry-a quirk that so intrigued medical students after Benjy's birth that they would crowd around the baby and try to make him cry. "Benjy was a pretty big item in the hospi­tal;' his mother says with a grin.

Dark blue lips and fingernails are the only traces of Martin Fugate's legacy left in the boy; that, and the re­cessive gene that has shaded many of the Fugates and their kin blue for the past 162 years. 

They're known simply as the "blue people" in the hills and hol­lows around Troublesome and Ball Creeks. Most lived to their 80s and 90s without serious illness associ­ated with the skin discoloration. For some, though, there was a pain not seen in lab tests. That was the pain of being blue in a world that is mostly shades of white to black.

There was always speculation in the hollows about what made the blue people blue-heart disease, a lung disorder; the possibility pro­posed by one old-timer that "their blood is just a little closer to their skin." But no one knew for sure, and doctors rarely paid visits to the remote creek side settlements where most of the "blue Fugates" lived until well into the 1950s. By the time a young hematologist from the University of Kentucky came down to Troublesome Creek in the 1960s to cure the blue peo­ple, Martin Fugate's descendants had multiplied their recessive genes all over the Cumberland Plateau.

Madison Cawein began hearing rumors about the blue people when he went to work at the Uni­versity of Kentucky's Lexington medical clinic in 1960. "I'm a hema­tologist, so something like that perks up my ears," Cawein says, sip­ping on whiskey sours and letting his mind slip back to the summer he spent "tromping around the hills looking for blue people."

Some blue people thought the doctor was addled for suggesting a blue dye could turn them pink.

Cawein is no stranger to eccen­tricities of the body. He helped iso­late an antidote for cholera, and he did some of the early work, on L-dopa, the drug for Parkinson's disease. But his first love, which he developed as an Army medical technician in World War II, was hematology. "Blood cells always looked so beautiful to me," he says.

Cawein would drive back and forth between Lexington and Haz­ard—an eight-hour ordeal before the toll way was built—and scour the hills looking for the blue people he'd heard rumors about. The American Heart Association had a clinic in Hazard, and it was there that Cawein met "a great big nurse" who offered to help.

Her name was Ruth Pendergrass, and she had been trying to stir UP medical interest in the blue people ever since a dark blue woman, walked into the county health department one bitterly cold after-noon and asked for a blood test.

"She had been out in the cold and' she was just blue!" recalls Pender­ grass, who is now 69 and retired from nursing. "Her face and her fingernails were almost' indigo blue. It like to scared me to death! She looked like she was having a heart attack. I just knew that patient was going to die right there in the health department, but she wasn't a'tall alarmed. She told me that her family was the blue Combses who lived up on Ball Creek. She was a sister to one of the Fugate women."

About this same time, another of the blue Combses, named Luke, had taken his sick wife up to the clinic at \_Lexington. One look at Luke was enough to "get those doc­tors down here in a hurry," says Pendergrass, who joined Cawein to look for more blue people.

Trudging up and down the hol­lows, fending off "the two mean dogs that everyone had in their front yard," the doctor and the nurse would spot someone at the top of a hill who looked blue and take off in wild pursuit. By the time they’d get to the top, the person would be gone. Finally, one day when the frustrated doctor was idling inside the Hazard clinic, Pat­rick and Rachel Ritchie walked in.

'They were bluer'n hell," Cawein says. "Well, as you can imagine, I really examined them. After con­cluding that there was no evidence of heart disease, I said 'Aha!' I started asking them questions: 'Do you have any relatives who are blue?' Then I sat down and we be­gan to chart the family."

Cawein remembers the pain that showed on the Ritchie brother's and sister's faces. "They were really embarrassed about being blue," he said. "Patrick was all hunched down in the hall. Rachel was lean­ing against the wall. They wouldn't come into the waiting room. You could tell how much it bothered them to be blue."

After ruling out heart and lung diseases, the doctor suspected methemoglobinemia, a rare hereditary blood disorder that results from excess levels of methemoglo­bin in the blood. Methemoglobin, which is blue, is a nonfunctional form of the red hemoglobin that carries oxygen. It is the color of oxygen-depleted blood seen in the blue veins just below the skin.

If the blue people did have methemoglobinemia, the next step was to find out the cause. It can be brought on by several things: ab­normal hemoglobin formation, an enzyme deficiency, and taking too much of certain drugs, including vitamin K, which is essential for blood clotting and is abundant in pork liver and vegetable oil.

Cawein drew "lots of blood" from the Ritchies and hurried back to his lab. He tested first for abnor­mal hemoglobin, but the results were negative.

Stumped, the doctor turned to the medical literature for a clue. He found references to methemoglob­incmia dating to the turn or the century, but it wasn't until he came across E. M. Scott's EJGO report in the journal of Clinical Investigation that the answer began to emerge.

Scott was a Public Health Service doctor at the Arctic Health Re­search Center in Anchorage who had discovered hereditary methe­moglobinemia among Alaskan Es­kimos and Indians. It was caused, Scott speculated, by an absence of the enzyme diaphorase from their red blood cells. In normal people hemoglobin is converted to methe­moglobin at a very slow rate. If this conversion continued, all the body's hemoglobin would eventu­ally be rendered useless. Normally diaphorase converts methemoglo­bin back to hemoglobin. Scott also concluded that the condition was inherited as a simple recessive trait. In other words, to get the disorder, a person would have to inherit two genes for it, one from each parent. Somebody with only one gene would not have the condition but could pass the gene to a child.

Scott's Alaskans seemed to match Cawein's blue people. If the condition were inherited as a reces­sive trait, it would appear most often in an inbred line.

Cawein needed fresh blood to do an enzyme assay. He had to drive eight hours back to Hazard to search out the Ritchies, who lived in a tapped-out mining town called Hardburly. They took the doctor to see their uncle, who was blue, too. While in the hills, Cawein drove over to see Zach (Big Man) Fugate, the 76-year-old patriarch of the clan on Troublesome Creek. His car gave out on the dirt road to Zach's house, and the doctor had to borrow a Jeep from a filling station.

"If you'll notice," Stacy says, tracing family lines on a chart, "I'm kin to myself."

Zach took the doctor even far­ther up Copperhead Hollow to see his Aunt Bessie Fugate, who was blue. Bessie had an iron pot of clothes boiling in her front yard, but she graciously allowed the doc­tor to draw some of her blood.

"So 1 brought back the new blood and set up my enzyme assay," Ca­wein continued. "And by God, they didn't have the enzyme diaphorase. I looked at other enzymes and nothing was wrong with them. So I knew we had the defect defined."

Just like the Alaskans, their blood had accumulated so much of the blue molecule that it over­whelmed the red of normal hemo­globin that shows through as pink in the skin of most Caucasians.

Once he had the enzyme defi­ciency isolated, methylene blue sprang to Cawein's mind as the "perfectly obvious" antidote. Some of the blue people thought the doc­tor was slightly addled for sug­gesting that a blue dye could turn them pink. But Cawein knew from earlier studies that the body has an alternative method of converting methemoglobin back to normal. Activating it requires adding to the blood a substance that acts as an "electron donor." Many substances do this, but Cawein chose methyl­ene blue because it had been used successfully and safely in other cases and because it acts quickly.

Cawein packed his black bag and rounded up Nurse Pendergrass for the big event. They went over to Patrick and Rachel Ritchie's house and injected each of them with 100 milligrams of methylene blue.

"Within a few minutes, the blue color was gone from their skin;' the doctor said.”For the first time in their lives, they were pink. They were delighted." "They changed colors!" remem­bered Pendergrass. "It was really something exciting to see." The doctor gave each blue family a supply of methylene blue tablets to take as a daily pill. The drug's ef­fects are temporary, as methylene blue is normally excreted in the urine. One day, one of the older mountain men cornered the doc­tor. "I can see that old blue running out of my skin," he confided.

Before Cawein ended his study of the blue people, he returned to the mountains to patch together the long and twisted journey of Martin Fugate's recessive gene. From a history of Perry County and some Fugate family Bibles list­ing ancestors, Cawein has con­structed a fairly complete story.

Martin Fugate was a French or­phan who immigrated to Kentucky in 1820 to claim a land grant on the wilderness banks of Troublesome Creek. No mention of his skin color is made in the early histories of the area, but family lore has it that Martin himself was blue.

The odds against it were incal­culable, but Martin Fugate man­aged to find and marry a woman who carried the same recessive gene. Elizabeth Smith, apparently, was as pale-skinned as the moun­tain laurel that blooms every spring around the creek hollows.

Martin and Elizabeth set up housekeeping on the banks of Troublesome and began a family. Of their seven children, four were reported to be blue.

The clan kept multiplying. Fu­gates married other Fugates. Sometimes they married first cous­ins. And they married the people who lived closest to them, the Combses, Smiths, Ritchies, and Stacys. All lived in isolation from the world, bunched in log cabins up and down the hollows, and so it was only natural that a boy married the girl next door, even if she had the same last name.

"When they settled this country back then, there was no roads. It was hard to get out, so they inter­married," says Dennis Stacy, a 51-year-old coal miner and ama­teur genealogist who has filled a loose-leaf notebook with the labori­ously traced blood lines of several local families.

Stacy counts Fugate blood in his own veins. "If you’ll notice," he ob­serves, tracing lines on his family's chart, which lists his mother's and his father's great grandfather as Henley Fugate, "I'm kin to myself."

The railroad didn't come through eastern Kentucky until the coal mines were developed around 1912, and it took another 30 or 40 years to lay down roads along the local creeks.

Martin and Elizabeth Fugate's blue children multiplied in this nat­ural isolation tank. The marriage of one of their blue boys, Zacha­riah, to his mother's sister trig­gered the line of succession that would result in the birth, more than 100 years later, of Benjy Stacy.

When Benjy was born with pur­ple skin, his relatives told the per­plexed doctors about his great grandmother Luna Fugate. One relative describes her as "blue all over;' and another calls Luna "the bluest woman I ever saw."

Luna's father, Levy Fugate, was one of Zachariah Fugate's sons. Levy married a Ritchie girl and bought 200 acres of rolling land along Ball Creek. The couple had eight children, including Luna.

A fellow by the name of John E. Stacy spotted Luna at Sunday ser­vices of the Old Regular Baptist Church back before the century turned. Stacy courted her, married her, and moved over from Trouble­some Creek to make a living in tim­ber on her daddy's land.

Luna has been dead nearly 20 years now, but her widower sur­vives. John Stacy still lives on Lick Branch of Ball Creek. His two­-room log cabin sits in the middle of Laurel Fork Hollow. Luna is buried at the top of the hollow. Stacy's son has built a modern house next door, but the old logger won't hear of leaving the cabin he built with timber he personally cut and hewed for Luna and their 13 children.

Stacy recalls that his father-in-law, Levy Fugate, was "part of the family that showed blue. All them old fellers way back then was blue. One of 'em - I remember seeing him when I was just a boy-Blue Anze, they called him. Most of them old people went by that name -the blue Fugates. It run in that generation who lived up and down Ball [Creek]."

"They looked like anybody else, 'cept they had the blue color," Stacy says, sitting in a chair in his plaid flannel shirt and suspenders, next to a cardboard box where a small black piglet, kept as a pet, is squeal­ing for his bottle. "I couldn't tell you what caused it."

The only thing Stacy can't-or won't-remember is that his wife Luna was blue. When asked about it, he shakes his head and stares steadfastly ahead. It would be hard to doubt this gracious man except that you can't find another person who knew Luna who doesn't re­ member her as being blue.

"The bluest Fugates 1 ever saw; was Luna and her kin;' says Carrie Lee Kilburn, a nurse who works at the rural medical center called: Homeplace Clinic.”Luna was bluish all over. Her lips were as dark as' a bruise. She was as blue a woman as I ever saw."

Luna Stacy, possessed the good health common to the blue people, bearing at least 13 children before she died at 84. The clinic doctors only saw her a few times in her life and never for anything serious.

 As coal mining and the railroads brought progress to Kentucky, the blue Fugates started moving out of their communities and marrying other people. The strain of inher­ited blue began to disappear as the recessive gene spread to families where it was unlikely to be paired with a similar gene.

Benjy Stacy is one of the last of the blue Fugates. With Fugate blood on both his mother's and his father's side, the boy could have re­ceived genes for the enzyme defi­ciency from either direction. Be­cause the boy was intensely blue at birth but then recovered his nor­mal skin tones, Benjy is assumed to have inherited only one gene for the condition. Such people tend to be very blue only at birth probably because newborns normally have smaller amounts of diaphorase. The enzyme eventually builds to normal levels in most children and to almost normal levels in those like Benjy, who carry one gene.

Hilda Stacy is fiercely protective of her son. She gets upset at all the talk of inbreeding among the Fu­gates. One of the supermarket tab­loids once sent a reporter to find out about the blue people, and she was distressed with his preoccupa­tion with intermarriages.

She and her husband Alva have a strong sense of family. They sing in the Stacy Family Gospel Band and have provided their children with a beautiful home and a menagerie of pets, including horses.

"Everyone around here knows about the blue Fugates," says Hilda Stacy who, at 26, looks more like a sister than a mother to her chil­dren. "It's common. It's nothing."

Cawein and his colleagues pub­lished their research on hereditary diaphorase deficiency in the *Ar­chives of Internal Medicine* in 1964. He hasn't studied the condition for years. Even so, Cawein still gets calls for advice. One came from a blue Fugate who'd joined the Army and been sent to Panama, where his son was born bright blue. Cawein advised giving the child methylene blue and not worrying about it.

The doctor was recently ap­proached by the producers of the television show "That's Incredible." They wanted to parade the blue people across the screen in their weekly display of human oddities. Cawein would have no part of it, and he related with glee the news that a film crew sent to Kentucky from Hollywood fled the "two mean dogs in every front yard" without any film. Cawein cheers their bad luck not out of malice but out of a deep respect for the blue people of Troublesome Creek.

"They were poor people," con­curs Nurse Pendergrass', "but they were good." \_

## STUDENT REFERENCE

### The Genetics of Parenthood Guidebook

Why do people, even closely related people, look slightly different from each other? The reason for these differences in physical characteristics (called phenotype) is the different combination of genes possessed by each individual.

To illustrate the tremendous variety possible when you begin to combine genes, you and a classmate will establish the genotypes for a potential offspring. Your baby will receive a random combination of genes that each of you, as genetic parents, will contribute. Each normal human being has 46 chromosomes (23 pairs - **diploid**) in each body cell. In forming the gametes (egg or sperm), one of each chromosome pair will be given, so these cells have only 23 single chromosomes (haploid). In this way, you contribute half of the genetic information (**genotype**) for the child; your partner will contribute the other half.

Because we don't know your real genotype, we'll assume that you and your partner are heterozygous for every facial trait. Which one of the two available alleles you contribute to your baby is random, like flipping a coin. In this lab, there are 36 gene pairs and 30 traits, but in reality there are thousands of different gene pairs, and so there are millions of possible gene combinations!

## Procedures

Record all your work on each parent's data sheet.

 First, determine your baby's gender. Remember, this is determined entirely by the father. The mother always contributes an X chromosome to the child.

* + Heads = X chromosome, so the child is a GIRL

Tails = Y chromosome, so the child is a BOY

Fill in the results on your data sheet.

 Name the child (first and middle name; last name should be the father's last name).

Determine the child's facial characteristics by having each parent flip a coin.

* + Heads = child will inherit the first allele (i.e. B or N1) in a pair

Tails = child will inherit the second allele (i.e. b or N2) in a pair

On the data sheet, circle the allele that the parent will pass on to the child and write the child's genotype.

 Using the information in this guide, look up and record the child's phenotype and draw that section of the face where indicated on the data sheet.

 Some traits follow special conditions, which are explained in the guide.

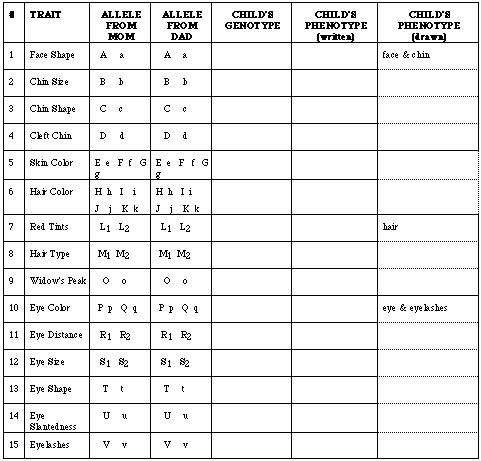
 When the data sheet is completed, draw your child's portrait as he/she would look as a teenager. You must include the traits as determined by the coin tossing. Write your child's full name on the portrait.

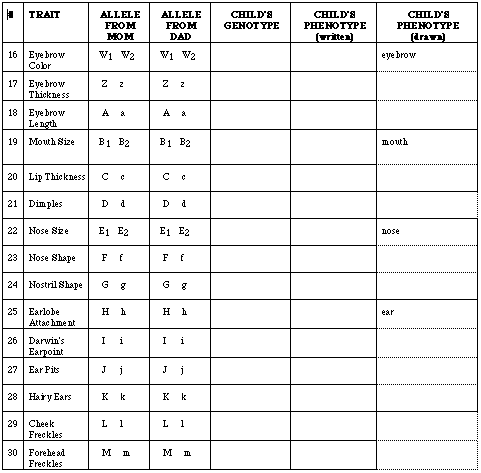
## STUDENT WORKSHEET

**The Genetics of Parenthood Data Sheet**

Parents \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ and \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Child's gender \_\_\_\_\_ Child's name \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Fill in data table as you determine each trait described in the Guidebook. Do not simply flip the coin for all traits before reading the guide, because some traits have special instructions. Believe it or not, it will make your life easier if you follow directions. In the last column, combine the information and draw what that section of the child's face would look like. 



## Questions:

1. What percentage does each parent contribute to a child's genotype?
2. Explain how/what part of your procedures represents the process of meiosis.
3. Using examples from this activity, explain your understanding of the following inheritance patterns:

a. dominant  
b. recessive  
c. incomplete dominance  
d. polygenic

1. Compare the predicted phenotype ratio (Punnett squares) to the actual ratio (class data) for the following traits:

a. trait # 2 (chin size)  
b. trait #8 (hair type)

1. All the children had 2 heterozygous parents. Use the law of independent assortment to explain why there were no identical twins produced.
2. One partner is responsible for drawing the face of the offspring and the other person write a biography of the child at age 30 – What the child is like, what have they accomplished and what their dreams are. (At least one page long.)

